5:00

764-5 Microvascular Integrity Preserves Contractile Reserve in Post-Infarction Dysfunctioning Myocardium

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In post myocardial infarction (MI) dysfunctioning segments (S), contrast enhancement observed during myocardial contrast echo (MCE) is an indicator of anatomic microvascular integrity. To investigate the functional effect of preserved microvasculature in maintaining myocardial contractile reserve, 13 pts were studied soon after acute MI (≤10 days) by (1) intracoronary MCE and (2) omniplane transesophageal echo (TEE) LV imaging in baseline conditions (B) and during low dose dobutamine infusion (5 mcg/kg/m' for 5' and 10 mcg/kg/m' for 5') (D). MCE was performed by injecting sonicated ioxaglate in both coronaries. A 13 S model was used for LV analysis both at MCE and TEE. In 40 dysfunctioning S (a- or severely hypo-kinetic) with excellent MCE and TEE imaging, myocardial thickening (%Th) was evaluated at B and during D. These 40 S were divided in 2 groups according to MCE results: 12 S without contrast enhancement (G1), 28 S with contrast enhancement (G2). Among the 28 S with contrast enhancement 18 S had contrast enhancement after contrast injection in the infarcted related artery (IRA), while the remaining 10 after injection in collateral circulation (CC) in the presence of occluded IRA.

Results:

	S (n)	B %Th	D %Th		S (n)	B %Th	D %Th	
G1	12	7.7 ± 12.5	12.4 ± 16.6	ns	IRA 18	18.9 ± 13.5	25.4 ± 17	ns
G2	28	20.2 ± 11.8	28.7 ± 14.8	**	CC 10	22.4 ± 8.3	34.6 ± 6.6	ns
		*						

n = number of S; * = $p < 0.001$ vs G2; ** = $p < 0.0001$ vs B. D vs B in G1 = ns

Conclusion: in post MI dysfunctioning S with microvascular integrity, as assessed by MCE, myocardial viability and contractile reserve are preserved. In fact, dysfunctioning S in the infarct area with contrast enhancement have greater %Th than S without, not only at B, but also during low dose D infusion. Both IRA and CC supply to dysfunctioning myocardium with microvasculature integrity are effective in preserving contractile reserve.

5:15

764-6 Effect of a New Phase Shift Echo Contrast Agent on Myocardial Blood Flow and Hemodynamics

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We have demonstrated the accuracy of myocardial area at risk and infarct size determinations with an emulsion of dodecafluoropentane (EchoGen ≈ EG) which is liquid at room temperature and a gas at body temperature (AHA meeting). To determine the effect of EG on myocardial blood flow (MBF), 10 fully anesthetized dogs received 4 (30 min apart) or 8 (10 min apart) peripheral intravenous injections of EG 0.5 ml/kg. HR, BP, T, PAP, PCWP, and CO were monitored. MBF was assessed with radiolabeled microspheres. Echo images were recorded with TEE. MBF (ml/min/g, ± SEM) was determined in four slices of the left ventricle (LV). Serial assessments of LV wall motion were performed.

	MBF Base	MBF Final
Anterior wall	1.4 ± 0.05	1.2 ± 0.2
Septal wall	1.2 ± 0.2	1.2 ± 0.2
Lateral wall	1.5 ± 0.1	1.2 ± 0.2
Posterior wall	1.5 ± 0.2	1.2 ± 0.2

PCWP, CO, and MBF were unchanged following 4 doses of EG. Systemic hypotension was seen, similar to that observed during administration of other perfluorochemicals in dogs. Pulmonary hypertension and deterioration in LV function were seen with 8 doses at 10 min intervals (cumulative dose: 4.0 ml/kg).

Conclusion: Administration of EG at frequent intervals can lead to a significant increase in PAP and myocardial dysfunction. However, EG does not produce significant alteration of MBF or PAP when administered at 30 min intervals at dosages that permit determination of myocardial area at risk and infarct size in our canine preparation.

765 Cellular Mechanisms of Atherosclerosis and Vascular Injury

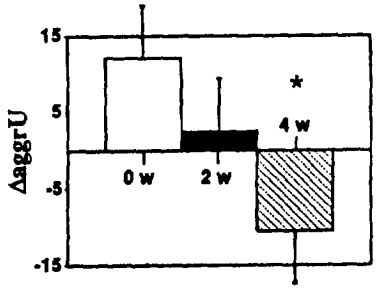
Tuesday, March 21, 1995, 4:00 p.m.–5:30 p.m.
Ernest N. Morial Convention Center, Room 61

4:00

765-1 Platelet Hyperaggregability in Hypercholesterolemic Humans: Reversal by Dietary L-Arginine

Christoff Zalpour, Gregor Theilmeier, Adrian Ma, Andreas Wolf, Barbara Anderson, Philip S. Tsao, John P. Cooke. *Stanford University, Stanford, CA*

We have shown that vascular NO activity is reduced in hypercholesterolemic animals, and that this abnormality can be reversed by dietary L-arginine (Arg) supplementation. A sustained improvement in vascular NO activity is associated with a reduction in platelet reactivity and elevation of platelet cGMP that is reversed by NO synthase inhibition. This study tested the hypothesis that chronic Arg supplementation would inhibit platelet reactivity in hypercholesterolemic humans. Venous blood was collected from normal (NC; n = 11) and hypercholesterolemic (HC; n = 22) volunteers for isolation of platelet-rich plasma and aggregometry. Half the HC group received Arg (8.4 g/d) for 2 weeks; aggregometry was performed using collagen (5 μg/ml) before and after 2 wks of treatment, and after a 2-wk washout.



Results: HC platelets were hyperaggregable (71 ± 3 v 56 ± 6 aggregation units [au]; HC v NC; $p < 0.03$). After 2 wks of Arg, HC platelets were no different in reactivity (64 ± 7 v 61 ± 6 au). This decrease of aggregability was sustained for 2 wks after discontinuing Arg (47 ± 9 v 60 ± 5 au; HC v NC). Figure shows change in au over time in HC-treated v untreated subjects.

Conclusion: These studies are consistent with our previous observations in animals that Arg inhibits platelet reactivity. The effect of Arg is likely mediated by its conversion to NO.

4:15

765-2 Dietary L-Arginine Attenuates Macrophage Infiltration and Intimal Hyperplasia After Balloon Injury

Robert C. Candipan, Bing-yin Wang, Paul T.C. Hsiun, Merhdad Arjomandi, Philip S. Tsao, John P. Cooke. *Stanford University, Stanford, CA*

Balloon injury in arteries of hypercholesterolemic animals creates a myointimal lesion that is comprised of macrophages as well as vascular smooth muscle cells. We have shown that chronic administration of L-arginine (Arg) enhances endothelial NO production and inhibits both monocyte-vessel wall interaction and plaque formation. Accordingly, we hypothesized that dietary Arg would reduce lesion formation and macrophage infiltration in hypercholesterolemic animals following balloon injury. NZW rabbits were divided into 3 groups: Normal chow (N), 0.5% cholesterol (Chol), or 0.5% Chol +2.25% Arg supplementation. Treatment was initiated 6 weeks prior to balloon injury of the left iliac artery. Four weeks after injury, the iliacs were harvested for: assessment of endothelium-dependent relaxation by vasodilation to acetylcholine; histology; and immunohistochemistry to assess macrophage infiltration. Endothelium-dependent relaxation was impaired following injury in the Chol and Arg groups (32 v 4 v 2%, N v Chol v Arg). In the contralateral non-injured arteries, Arg treatment restored endothelium-dependent relaxation (79 v 44 v 64%, N v Chol v Arg). The Chol group showed a 2.5-fold increase in intimal area following injury compared with N, while Arg attenuated lesion formation (0.28 v 0.69 v 0.34 mm^2, N v Chol v Arg, $p < 0.01$). Area involved by macrophage increased in the Chol iliacs compared with N, while Arg significantly attenuated macrophage infiltration (2 v 28 v 5%, N v Arg v Chol, $p < 0.001$).

Conclusion: Chronic arginine supplementation reduces intimal proliferation and attenuates macrophage infiltration following balloon injury in hypercholesterolemic animals, and is associated with restored NO-dependent vasodilation.

TUESDAY PM